A CASE WITH THE SYMPTOMS OF CEREBRO-SPINAL MENINGITIS, WITH INTENSE AND GENERAL ALTERATION OF THE NERVE CELL-BODIES, BUT WITH LITTLE EVIDENCE OF INFLAMMATION.[1]

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The following case is interesting because symptoms of meningitis existed for six days and yet lesions sufficient to explain these symptoms were not found at the necropsy. The intense and general alteration of the nerve cell-bodies suggests some remarks relative to the similar lesions observed in amaurotic family idiocy.

According to the records in the case-books of the Pennsylvania Training School for Feeble-Minded Children, F. S. M. was born July 11, 1892, and was admitted to the Training School, March 19, 1900. The parents of the child are living and in good health. The father, a teamster, was thirty-two years of age, and the mother twenty-six at the birth of this their fifth child. There is no history of intemperance in parents or grandparents. F. was born at full term, but in difficult labor, lasting three days. One brother and one sister of the boy are living, and are healthy, mentally and physically. F. was of feeble mental development; he did not know the alphabet, did not talk and could not dress himself properly. His sight and hearing were good. His gait was spastic. He was of small size, and had scoliosis. Sensation was normal so far as could be determined. He did not have convulsions.

The following notes were made by Dr. W. G. Shallcross, the resident physician:

"April 1, 1900. I was called early this morning to see F. and found him in considerable pain, which he could not locate. The skin was hot and dry, pulse was rapid and he had diarrhea and vomiting. In the afternoon he was not so restless. The bowels had moved once. The heart's action was rapid and the second sound was accentuated, but there was no murmur.

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[1] From the Wm. Pepper Clinical Laboratory, Phœbe A. Hearst Foundation.

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The condition of the lungs was normal. The liver and spleen were not enlarged. Urine was passed involuntarily.

"April 2. F. was not so well to-day. He was more restless, but it was impossible to determine the location of the pain. The abdominal muscles were rigid, but showed no tenderness on pressure. He retained food.

"April 3. He was very restless and the skin was hypersensitive. The pupils were equal and seemed to react sluggishly. He had some photophobia. The abdominal muscles were rigid and the legs were drawn up on the abdomen as if the boy were in pain.

"April 4. Photophobia was quite pronounced. The pupils were about 3 mm., equal, and did not react to light. The neck was somewhat rigid and the head was retracted slightly. The muscles of all the extremities were stiff and the hands were thrown about wildly when the patient was disturbed. Hyperesthesia was very pronounced. The thighs were frequently flexed upon the abdomen.

"April 5. F. had a very restless night and was delirious at times. An erythema was noticed this morning about the right knee and calf. No albumin was found in the urine.

"April 6. Coma is developing and the patient is more quiet. The rash is spreading. He could not take food and was nourished by the rectum. Death occurred at 9.30 P. M."

A diagnosis of cerebro-spinal meningitis was made by Dr. Shallcross.

The necropsical notes are as follows: Cadaveric rigidity was present. Numerous small, dark-reddish spots of various sizes and shapes were seen on the anterior surfaces of the thighs, on the outer and inner parts of the legs below the knees, and on the anterior surfaces of the upper limbs.

Brain: The scalp was very adhesive to the skull. The cerebral dura was adherent to the calvarium at the coronal and sagittal sutures. A large amount of cerebro-spinal fluid tinged with blood escaped when the calvarium was removed. The brain was edematous. The superior longitudinal sinus contained a few soft clots. The dura was slightly adherent to the pia in small areas at the anterior part of the right frontal lobe and at the right temporal convolutions. No distinct evidences of inflammation could be detected with the naked eye. The pia about the optic chiasm and covering the interpeduncular space was somewhat opaque in patches, but hardly more than is seen in many normal brains. No miliary tubercles could be found.

Heart was small, normal in position, and the pericardial fluid was not excessive. Right auricle and pulmonary artery contained chicken-fat clots. Tricuspid valve admitted two fingers and was normal. Mitral valve admitted the middle finger easily. Left auricle did not contain any clot. A chicken-fat clot was found in the right ventricle. The mitral and aortic valves appeared to be thickened. The cardiac muscle was a little pale.

Lungs: Right lung was somewhat edematous, but crepitated, and did not contain any areas of consolidation. The left lung was in the same condition as the right. There were no pleural adhesions on the left side, but some old adhesions were found on the right side. The diaphragm extended to the fourth rib on each side.

Liver was of good size and smooth, and extended to the border of the last rib. Reddish spots were seen on the upper surface, especially on the left lobe. The tissue was somewhat yellow on section and numerous small reddish areas like hemorrhages were found. The gall bladder was full.

Spleen was of normal size and of dark slate color. A small supernumerary spleen was found.

Pancreas appeared to be normal.

Suprarenals appeared to be normal.

L. Kidney: Capsule stripped easily and the surface of the kidney was smooth. No cysts were found. The tissue was pale on section; the cortex was somewhat yellowish. The pyramids were fairly distinct. The right kidney was in the same condition as the left.

Stomach was congested and small hemorrhages were found on its inner surface.

Bladder was normal and filled with urine.

Weight of brain, 1,040 grm.; heart, 80 grm.; left lung, 165 grm.; right lung, 175 grm.; left kidney, 75 grm.; right kidney, 65 grm.; liver, 810 grm.; spleen, 90 grm.

It is not surprising that this case was diagnosticated as one of cerebro-spinal meningitis, on account of the acute onset of the disease with fever of 102 degrees F., diarrhea and vomiting; the pain, the rigidity of the abdominal muscles, the hyperesthesia of the skin, the photophobia, the stiffness of the neck, etc. The microscopical examination of the nervous tissues, however, showed little evidence of inflammation. The nerve cell-bodies throughout the central nervous system were greatly altered and this alteration was not confined to the cells with motor function. It was seen in the cell-bodies of the posterior and anterior horns of the spinal cord, in the nuclei of the cranial nerves, in the sensory, as well as the motor, nucleus of the fifth nerve; in the cells of Purkinje and in the parietal lobule, where especially the cells of Betz were altered. The cell-body was swollen and rounded; many of the dendritic processes had disappeared; the chromophilic elements were not to be seen, except in one portion of the cell-body, where they surrounded the nucleus, and even here were more or less disintegrated, and the nucleus had moved to the periphery of the cell-body. This description applies to most of the nerve cell-bodies of the central nervous system. The appearance presented by the cell-bodies of the anterior horns

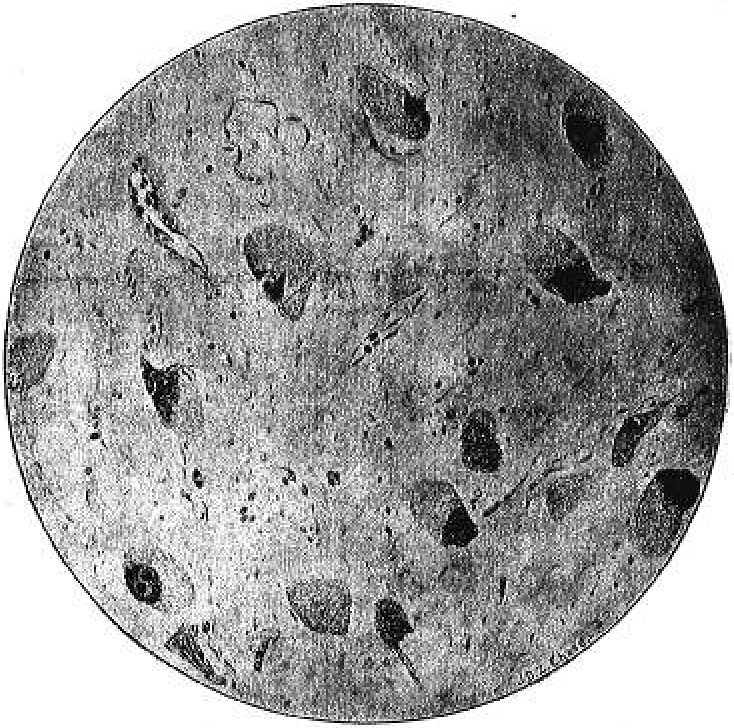

Fig. I. Cell-bodies of the anterior horns in the lumbar region. They are represented as they appear in *one* field of the microscope, in order to show the intense alteration of all the cell-bodies.

was most extraordinary, as all the cell-bodies had undergone this peculiar alteration (Figs. I. and II.).

The lesions of meningitis were not found. A very slight round-cell infiltration was observed in some parts of the pia (Fig. III.) and about some of the intramedullary blood vessels, but the small vessels of the pia and anterior and posterior roots were much distended with blood. Numerous small bacilli were found within the nervous tissues.

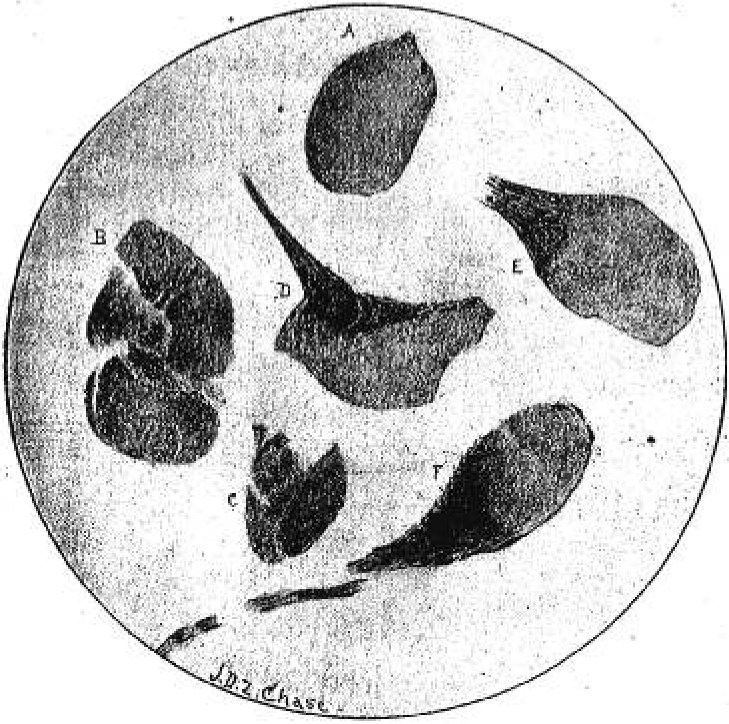

Fig. II. Selected cell-bodies from the anterior horns of the lumbar region, with the exception of cell-body E, which is from the paracentral lobule. Cell-body A shows complete chromatolysis. The cell-bodies B and C are divided into several parts. In D, E and F the chromophilic elements are seen in only one part of the cell-body, and the nucleus is not distinct.

In a case of amaurotic family idiocy Hirsch[2] observed a very extraordinary change in the nerve cell-bodies of the central nervous system. All the cell-bodies of the anterior and posterior horns were greatly enlarged and round. The nucleus was at the periphery of the cell-body and was sharply defined, and contained a nucleolus staining deeply. The nucleus was surrounded by a dark zone gradually shading off into a more or less colorless area. The dark zone contained broken-down chromophilic elements and occasionally a few normal ones. The light area of the cell-body was made up of a very fine network. Some of the cell-bodies were vacuolated. The dendrites and axone of the cell were very few, and many of the processes seemed to be broken off. The pictures of these cell-bodies represent them as swollen,

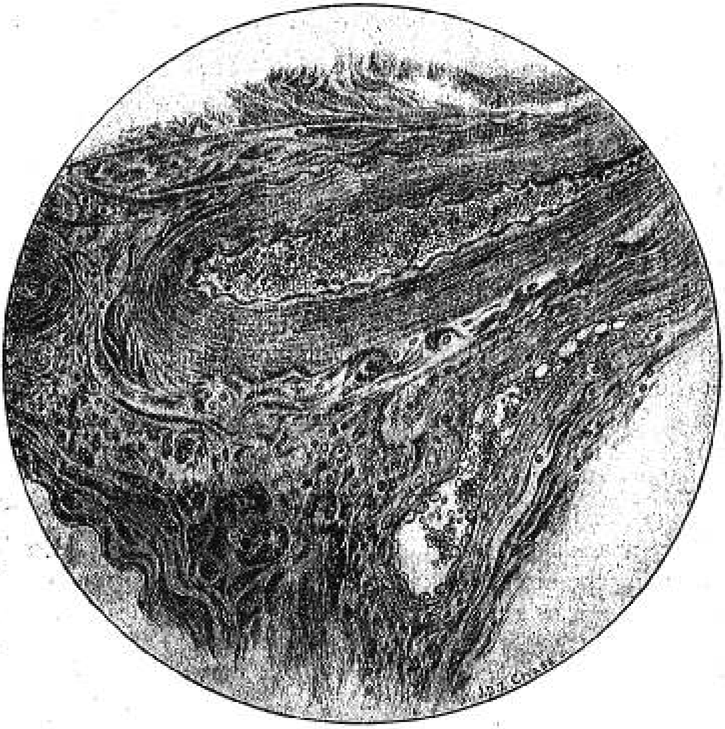

Fig. III. The pia of the anterior fissure of the spinal cord, showing a slight round-cell infiltration. Nowhere is the cellular infiltration more intense than that represented in the drawing.

almost round masses. The same alteration was found in all the cell-bodies of the central nervous system, although the cell-bodies of the cerebellum were not much affected. Hirsch found degeneration of the pyramidal tracts. When he examined some of the preparations from a case of amaurotic family idiocy reported previously by Sachs, he found in these a similar change of the nerve cell-bodies, although the material had been hardened in Müller's fluid. Hirsch refers to no cases that were not of amaurotic family idiocy, in which a similar change of all the nerve cell-bodies was found, and he states that no disease is known in which simultaneously all the nerve cell-bodies of the entire nervous system become affected. The condition of the nerve cell-bodies in his case, he thought, corresponded in every respect to that found after experimental poisoning, and amaurotic family idiocy is therefore an acquired disease and is produced by some poison, possibly by a toxic condition of the mother's milk.

Sachs[2] argued in the discussion of this paper that a disease so widespread as amaurotic family idiocy, which begins always at the same period of life, and attacks several members of the same family and leaves others exempt, could not be due to any toxic influence that is known to us. From this we may conclude that Sachs either did not regard the alteration of the nerve cell-bodies as of toxic origin, or else he thought that this cellular degeneration did not explain the disease. Hirsch, in closing the discussion on amaurotic family idiocy, remarked that the toxic origin of the disease was an open question. He knew of no other inherited family affection where all the nerve cell-bodies, and nothing but the nerve cell-bodies, became diseased, and the condition, so far as he knew, had no analogy in pathology.

I have seen this same general alteration of the nerve cell-bodies of the central nervous system in two cases, and neither was a case of amaurotic family idiocy. One was a case of internal hemorrhagic pachymeningitis in an idotic child aged nine years, and the microscopical report was published by me[3] in collaboration with Dr. D. J. McCarthy. Even by the carmine stain the alteration of the cell-bodies in preparations hardened in Müller's fluid was most striking. The pyramidal tracts were not degenerated, which is interesting in view of the intense alteration of the motor cell-bodies. In Hirsch's case these tracts were degenerated.

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[2] Hirsch, Sachs. THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1898, No. 7, pp. 538, 555.

[3] Spiller and McCarthy. THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1899, No. 11, p. 677.

The second case in which I have observed this intense and general alteration of the nerve cell-bodies of the central nervous system is the one with symptoms of cerebro-spinal meningitis reported in this paper. It is noteworthy that the cellular alteration in these two cases was in children of feeble mental development, as in the cases of amaurotic family idiocy, and such cellular alteration is therefore not confined to amaurotic family idiocy.

A theory of a toxic condition in the second case could be well supported by the clinical history, but not so well in the case of internal hemorrhagic pachymeningitis, although even in this it could not be absolutely rejected. The alteration of the nerve cell-bodies throughout the central nervous system is extraordinary, and yet in the two cases in which I have observed it secondary degeneration has not occurred. I am not aware that such an intense and widespread alteration of the cell-bodies of the central nervous system has been observed by other investigators in cases of disease of the human nervous system.

The symptoms of cerebro-spinal meningitis sometimes occur in typhoid fever and other infectious diseases without alteration of the meninges, and to this form of pseudo-meningitis the name of *meningisme* has been given by Dupré, and Schultze has spoken of "meningitis without meningitis." It is not impossible that in some of these cases an alteration of the nerve cell-bodies similar to that in my case occurs. A paper bearing on this subject has recently been published by Finkelstein.[4] He says a few cases of longer or shorter duration have been observed in which the symptoms were indicative of meningitis and were fever, convulsions, rigidity of the neck, hyperesthesia and opisthotonos, and yet at the necropsy only slight edema and softening of the brain and a small excess of ventricular cerebro-spinal fluid were found. He did not regard this condition as a true meningitis serosa, but as inflammatory cerebral edema, because cellular infiltration of the meninges has been observed in a few cases.

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[4] Finkelstein. Monatsschrift für Psychiatrie und Neurologie, Vol. 8, No. 4.

Finkelstein shares the opinion of Seitz that some toxic substance in the crebro-spinal fluid is the cause of this slight inflammatory edema, and that pathogenic bacteria in the cerebro-spinal fluid may cause severe cerebral symptoms without causing a distinct meningitis. He points out that in some cases meningitis serosa has been found to be due to the presence of bacteria. It seems that meningitis serosa cannot be sharply distinguished from the inflammatory cerebral edema.

It is important to remember that pronounced symptoms of meningitis may be present with very slight alteration of the meninges, and that even purulent meningitis may exist without any symptoms. In my case the brain was edematous, and on microscopical examination, very slight cellular infiltration could be found in the pia, so slight as to be questionable, but the nerve cell-bodies throughout the central nervous system were intensely altered, and yet there is doubt concerning the relation of this alteration of the nerve cell-bodies to the symptoms of meningitis.

Numerous bacteria were found within the nervous tissue of my case, reported in this paper, and while Dr. S. S. Kneass, to whom I showed a section, recognized them as short bacilli, he was unwilling to give them a name. The symptoms of the case and a slight perivascular round-cell infiltration would indicate that these bacilli were probably within the tissues before death, and yet the recent paper by Zappert[5] on the presence of micro-organisms within the spinal cord shows how difficult it is to decide whether a bacterial invasion has occurred before or after death. The intense alteration of the nerve cell-bodies in my case may possibly have been the result of a toxin, but it has not been demonstrated that this is the correct view.

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[5] Zappert. Obersteiner's "Arbeiten," Vol. 7.